PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

SCHWANDER Kuno Josef
c/o Roche Vitamins Ltd
Patent Department (VMD)
Wurmisweg 576
CH-4303 Kaiseraugst
SUISSE

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing *(day/month/year)*	08.09.2004

Applicant's or agent's file reference	IMPORTANT NOTIFICATION
Case 21516 WO	

International application No	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP 03/13665	04.12.2003	06.12.2002

Applicant
ROCHE VITAMINS AG

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:

European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized Officer

Morancho Alcaine, N

Tel. +49 89 2399-7462

Bitte sofort Literatur im Zedo eintragen und Fehlendes bestellen

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference Case 21516 WO	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/13665	International filing date *(day/month/year)* 04.12.2003	Priority date *(day/month/year)* 06.12.2002
International Patent Classification (IPC) or both national classification and IPC A61K31/01		
Applicant ROCHE VITAMINS AG		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
22.06.2004	08.09.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Loher, F Telephone No. +49 89 2399-7839

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/13665

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-14 as originally filed

Claims, Numbers

1-31 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 25-31 (IA)

   because:

   ☒ the said international application, or the said claims Nos. 25-31 (IA) relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	8, 9, 11, 17-21
	No:	Claims	1-7, 10, 12-16, 22-31
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-31
Industrial applicability (IA)	Yes:	Claims	1-24
	No:	Claims	

2. Citations and explanations

   see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 25-31 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: WO 01 22958 A (AVANSIS LTD ;CAREY ADAM HENRY (GB); CAREY BEVERLY JANE (GB); HAYNE) 5 April 2001 (2001-04-05)

D2: WO 02 058683 A (PARAN ESTER ;ZELKHA MORRIS (IL); LYCORED NATURAL PROD IND LTD (IL)) 1 August 2002 (2002-08-01)

D3: PARAN ESTHER ET AL: 'Effect of tomato's lycopene on blood pressure, serum lipoproteins, plasma homocysteine and oxidative stress markers in grade I hypertensive patients' AMERICAN JOURNAL OF HYPERTENSION, vol. 14, no. 4 Part 2, April 2001 (2001-04), page 141A XP002276573 Sixteenth Annual Scientific Meeting of the American Society of Hypertension;San Francisco, California, USA; May 15-19, 2001 ISSN: 0895-7061

D4: US 2002/155163 A1 (BENJAMIN SAMUEL D ET AL) 24 October 2002 (2002-10-24)

D5: DE 101 09 798 A (AVENTIS PHARMA GMBH) 12 September 2002 (2002-09-12)

D6: US 2002/001632 A1 (REVEL CHASE) 3 January 2002 (2002-01-03)

D7: EP-A-1 314 438 (NUTRICIA N V) 28 May 2003 (2003-05-28)

If not mentioned otherwise, the relevant passages are those mentioned in the International Search Report. Assuming a valid priority of the present application the E-document (D7) cited in the International Search Report is not dealt with during the PCT-phase.

Art 33(2) The present application does not meet the requirements of Article 33(2) PCT, since the subject-matter of claims 1-7, 10, 12-16 and 22-31 is not new.

D1 discloses the use of a composition comprising lycopene (10 mg), vitamin C (6000 mg) and vitamin E (600 mg) for the treatment of arterial hypertension. Therefore, the subject-matter of claims 1-5, 7, 13, 14, 25-28, 30 and 31 is not new in the light of D1.

D2 discloses the use of a composition comprising lycopene, vitamin C and vitamin E for the treatment of arterial hypertension. The efficacy of 15mg/die lycopene in reductiobn of blood pressure is demonstrated. Therefore, the subject-matter of claims 1, 2, 5, 7, 13, 14, 25-27, 30 and 31 is not new in the light of D2.

D3 discloses the efficacy of lycopene in the treatment of arterial hypertension. Therefore, the subject-matter of claims 1, 5, 7, 13, 14, 25-27, 30 and 31 is not new in the light of D3.

D4 discloses the use of a composition comprising lycopene (4-6 mg), vitamin C (100-500 mg) and vitamin E (260-580 mg) and vitamin D for the treatment of diabetes mellitus. Therefore, the subject-matter of claims 1-7, 10, 13-16 and 22-31 is not new in the light of D4.

D5 discloses the use of a composition comprising lycopene (5 mg), vitamin C (500 mg) and vitamin E (265 mg) for the treatment of diabetes mellitus. Therefore, the subject-matter of claims 1-7, 10, 13-16 and 22-31 is not new in the light of D5.

D6 discloses the use of a composition comprising lycopene (4-6 mg) and serenoa repens extract for the treatment of benign prostatic hyperplasia. Therefore, the subject-matter of claims 1, 4-7, 12-14, 19, 22, 25-27, 30 and 31 is not new in the light of D6.

Art 33(3) The present application does not meet the requirements of Article 33(3) PCT, since the subject-matter of claims 1-31 does not seem to involve an inventive step.

D4, which is considered to represent the most relevant state of the art, discloses the use of a composition comprising lycopene (4-6 mg), vitamin C (100-500 mg) and vitamin E (260-580 mg) and vitamin D for the treatment of diabetes mellitus.

The problem to be solved by the present invention may therefore be regarded as how to provide another medical use of lycopene.

The present application suggests to solve the problem posed by suggesting the use of lycopene in the treatment of non-cancerous diseases being associated with androgen signalling, such as polycystic ovary syndrome, feminine acne, hirsutism, benign prostatic hyperplasia, diabetes mellitus or hypertonia etc.

On a more abstract level the technical contribution to the state of the art suggested by the present application is a new medical use of known compounds. It must, thus, be of particular relevance that the compounds in question work over the whole range of the claimed use (i.e. lycopene must be efficient in the treatment of each mentioned disease).

Taking into account the teaching of the cited prior art the following reasoning applies:

With respect to the subject-matter of claims 1-7, 10, 12-16 and 22-31 the applicant's attention is drawn to the fact that even if novelty could be established over the above-cited prior art it is at present not clear wherein an inventive step may reside.

With respect to the subject-matter of claims 19-21 the applicant's attention is drawn to the fact that there seems to be no basis for inventive step within the present application as filed since no evidence can be found that the features which are novel over the prior art (liquid dosage forms) contribute to the solution of the posed problem.

With respect to the subject-matter of the remaining claims 8, 9, 11, 17 and 18 the applicant's attention is drawn to the fact that there seems to be no basis for inventive step within the present application as filed since no evidence can be found that the posed problem has been solved as it has not been shown that lycopene exerts any pharmacological effect that qualifies its use for the treatment of the claimed diseases.

It is therefore noted, that the solution proposed in claims 1-31 of the present application is not considered to be inventive in the sense of Article 33(3) PCT.

Art 33(4) For the assessment of the present claims 25-31 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

The subject-matter of claims 1-24 is considered to be industrially applicable in the sense of Art 33(4) PCT.